



Agency for Healthcare Research and Quality
Advancing Excellence in Health Care



NATIONAL
GUIDELINE
CLEARINGHOUSE

General

Guideline Title

Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement.

Bibliographic Source(s)

U.S. Preventive Services Task Force. Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013 Sep 3;159(5):349-57. [20 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Screening for hepatitis C virus infection in adults: recommendation statement. *Ann Intern Med.* 2004 Mar 16;140(6):462-4.

Recommendations

Major Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the levels of certainty regarding net benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Summary of Recommendations and Evidence

The USPSTF recommends screening for hepatitis C virus (HCV) infection in persons at high risk for infection. The USPSTF also recommends offering one-time screening for HCV infection to adults born between 1945 and 1965. (B recommendation)

Clinical Considerations

Patient Population under Consideration

This recommendation applies to all asymptomatic adults without known liver disease or functional abnormalities.

Assessment of Risk

The most important risk factor for HCV infection is past or current injection drug use. Another established risk factor for HCV infection is receipt of a blood transfusion before 1992. Because of the implementation of screening programs for donated blood, blood transfusions are no longer an important source of HCV infection. In contrast, 60% of new HCV infections occur in persons who report injection drug use within the past 6 months.

Additional risk factors include long-term hemodialysis, being born to an HCV-infected mother, incarceration, intranasal drug use, getting an unregulated tattoo, and other percutaneous exposures (such as in health care workers or from having surgery before the implementation of universal precautions). Evidence on tattoos and other percutaneous exposures as risk factors for HCV infection is limited. The relative importance of these additional risk factors may differ on the basis of geographic location and other factors.

Large population-based studies report an independent association between high-risk sexual behaviors (multiple sex partners, unprotected sex, or sex with an HCV-infected person or injection drug user) and HCV infection. However, HCV seems to be inefficiently transmitted through sexual contact, and observed associations may have been confounded by other high-risk behaviors.

In 1998, the highest prevalence rates of the anti-HCV antibody occurred in persons with significant direct percutaneous exposures, such as injection drug users and persons with hemophilia (60% to 90%); persons with less significant percutaneous exposures involving smaller amounts of blood, such as patients receiving hemodialysis (10% to 30%), had more moderate prevalence rates. Persons engaging in high-risk sexual behaviors (1% to 10%); recipients of blood transfusions (6%); and persons with infrequent percutaneous exposures, such as health care workers (1% to 2%), had the lowest prevalence rates.

Among patients with abnormal results on liver function tests (measurement of aspartate aminotransferase, alanine aminotransferase, or bilirubin) who were tested for reasons other than HCV screening, finding the cause of the abnormality often includes testing for HCV infection and is considered case finding rather than screening; therefore, it is outside the scope of this recommendation.

In 2010, the overall incidence rate of acute HCV infection was 0.3 case per 100,000 persons and varied by race or ethnicity. The incidence rate for acute hepatitis C was lowest among persons of Asian or Pacific Islander descent and highest among American Indians and Alaskan natives. Black persons had the highest mortality rates from HCV, at 6.5 to 7.8 deaths per 100,000 persons, according to data from 2004 to 2008.

Birth-Cohort Screening

Persons born between 1945 and 1965 are more likely to be diagnosed with HCV infection, possibly because they received blood transfusions before the introduction of screening in 1992 or have a history of other risk factors for exposure decades earlier. Many persons with chronic HCV infection are unaware of their condition. A risk-based approach may miss detection of a substantial proportion of HCV-infected persons in the birth cohort because of a lack of patient disclosure or knowledge about prior risk status. As a result, one-time screening for HCV infection in the birth cohort may identify infected patients at earlier stages of disease who could benefit from treatment before developing complications from liver damage.

The USPSTF concluded that the benefit of screening for HCV infection in persons in the birth cohort is probably similar to that in persons at higher risk for infection. Birth-cohort screening is probably less efficient than risk-based screening, meaning more persons will need to be screened to identify one patient with HCV infection. Nevertheless, the overall number of Americans who will probably benefit from birth-cohort screening is greater than the number who will benefit from risk-based screening.

The USPSTF recognizes that increased screening and the resulting increased diagnoses and treatment could result in increased overall harms because not all treated persons will benefit from treatment, including those who will never develop signs or symptoms of disease (overdiagnosis). The USPSTF weighed this potential harm against the potential harm of undertreatment attributable to underdiagnosis. It is hoped that future research will reduce overtreatment by clarifying which persons are most likely to benefit from early diagnosis and treatment. However, given that persons in the birth cohort have been living with HCV infection for 20 or more years, the potential benefit of screening and early treatment will probably be at its highest now and in the near future before becoming smaller. After weighing the competing harms of overtreatment and underdiagnosis, the USPSTF recommends one-time screening for this cohort.

Screening Tests

Anti-HCV antibody testing followed by polymerase chain reaction testing for viremia is accurate for identifying patients with chronic HCV infection. Various noninvasive tests with good diagnostic accuracy are possible alternatives to liver biopsy for diagnosing fibrosis or cirrhosis.

Screening Intervals

Persons in the birth cohort and those who are at risk because of potential exposure before universal blood screening and are not otherwise at increased risk need only be screened once. Persons with continued risk for HCV infection (injection drug users) should be screened periodically. The USPSTF found no evidence about how often screening should occur in persons who continue to be at risk for new HCV infection.

Screening Implementation

The USPSTF believes that screening should be voluntary and undertaken only with the patient's knowledge and understanding that HCV testing is

planned. Patients should be informed orally or in writing that HCV testing will be performed unless they decline (opt-out screening). The USPSTF further believes that before HCV screening, patients should receive an explanation of HCV infection, how it can (and cannot) be acquired, the meaning of positive and negative test results, and the benefits and harms of treatment. Patients should also be offered the opportunity to ask questions and to decline testing.

Treatment

The purpose of antiviral treatment regimens is to prevent long-term health complications of chronic HCV infection (such as cirrhosis, liver failure, and hepatocellular carcinoma).

The combination of pegylated interferon ($\alpha 2a$ or $\alpha 2b$) and ribavirin is the standard treatment for HCV infection. In 2011, the U.S. Food and Drug Administration approved the protease inhibitors boceprevir and telaprevir for the treatment of HCV genotype 1 infection (the predominant genotype in the United States). Trials have found increased sustained virologic response rates in patients with HCV genotype 1 infection who received triple therapy consisting of pegylated interferon, ribavirin, and boceprevir or telaprevir compared with dual therapy consisting of pegylated interferon and ribavirin. Evidence is lacking on the comparative effects of current antiviral treatments on long-term clinical outcomes. Regimens with protease inhibitors are usually of shorter duration than dual therapy (24 or 28 weeks vs. 48 weeks). Triple therapy with protease inhibitors is associated with an increased risk for hematologic events (such as anemia; neutropenia; and thrombocytopenia, particularly with boceprevir) and rash (telaprevir) compared with dual therapy. These adverse events are self-limited and typically resolve after the discontinuation of treatment.

Definitions:

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be measured.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:

Level of Certainty	Description
	<ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; and • Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; and • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hepatitis C virus infection

Guideline Category

Prevention

Screening

Treatment

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To update the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for hepatitis C virus infection in asymptomatic adults

Target Population

Persons at high risk for infection and adults born between 1945 and 1965 (applies to all asymptomatic adults without known liver disease or functional abnormalities)

Interventions and Practices Considered

Screening for hepatitis C virus (HCV) infection:

- Assessment of risk factors for infection, including current or past injection drug use or receipt of a blood transfusion before 1992
- Birth cohort screening of persons born between 1945 and 1965
- Use of anti-HCV antibody testing followed by polymerase chain reaction testing for viremia or other noninvasive tests with good diagnostic accuracy
- Screening intervals
- Screening implementation with informed voluntary consent
- Consideration of benefits and harms of antiviral therapy

Major Outcomes Considered

Screening

- Key Question 1: Does screening for hepatitis C virus (HCV) infection in nonpregnant adults without known abnormal liver enzymes reduce mortality and morbidity due to HCV infection, affect quality of life, or reduce incidence of HCV infection?
- Key Question 2: What is the effectiveness of different risk- or prevalence-based methods for screening for HCV infection on clinical outcomes?
- Key Question 3: What is the sensitivity and number needed to screen to identify 1 case of HCV infection of different risk- or prevalence-based methods for screening for HCV infection?
- Key Question 4: What are the harms associated with screening for HCV infection, including diagnostic liver biopsies?

Treatment

- Key Question 1: What is the comparative effectiveness of antiviral treatment in improving health outcomes in patients with HCV infection, and does it vary according to patient subgroup characteristics (including, but not limited to, HCV genotype, age, race, sex, stage of disease, or genetic markers)?
- Key Question 2: What is the comparative effectiveness of antiviral treatments on the rate of sustained virologic response (SVR), and does it vary according to patient subgroup characteristics?
- Key Question 3: What are the comparative harms associated with antiviral treatments, and do they vary according to patient subgroup characteristics?
- Key Question 4: Have improvements in SVR been shown to reduce the risk for or rates of adverse health outcomes from HCV infection?

Mother-to-Infant Transmission

Key Question: What is the effect of mode of delivery, labor management strategy, or breastfeeding on risk for mother-to-infant transmission of

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): Systematic evidence reviews were prepared by the Oregon Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Screening

Data Sources and Searches

A research librarian searched Ovid MEDLINE (1947 to May 2012), EMBASE, the Cochrane Library Database, Scopus, and PsycINFO; clinical trial registries (including ClinicalTrials.gov); and grants databases. Electronic searches were supplemented by reviewing reference lists of retrieved articles.

Study Selection

At least 2 reviewers independently evaluated each study to determine inclusion eligibility. Papers were selected for full review if they were relevant to a key question and met the predefined inclusion criteria. For screening, EPC staff included randomized trials, cohort studies, case-control studies, and cross-sectional studies that compared different screening strategies in asymptomatic adults without known liver enzyme abnormalities and reported clinical outcomes or sufficient information to compute the sensitivity and number needed to screen to identify 1 hepatitis C virus (HCV)-infected person. EPC staff also included large studies (sample size >1000 participants) reporting harms associated with diagnostic liver biopsy published since 2004 and uncontrolled or controlled studies reporting direct harms associated with screening.

Clinical outcomes were mortality, end-stage liver disease, cirrhosis, hepatocellular carcinoma, need for transplantation, quality of life, HCV transmission, harms associated with screening (such as anxiety, labeling, and effects on quality of life), and harms associated with liver biopsy (including death, bleeding, and severe pain).

EPC staff restricted inclusion to English-language articles and excluded studies published only as abstracts. They excluded studies of posttransplant patients, human immunodeficiency virus (HIV)-infected patients, patients undergoing hemodialysis, and persons with occupational exposures, in whom screening and treatment considerations may differ from those in the general population.

Treatment

Data Sources and Searches

A research librarian searched Ovid MEDLINE from 1947 to August 2012, the Cochrane Library Database (through the first quarter of 2012), EMBASE (1976 to August 2012), Scopus (1960 to August 2012), PsycINFO (1806 to August 2012), clinical trials registries, and grants databases.

Study Selection

At least 2 reviewers independently evaluated studies for inclusion. For the first three questions, EPC staff included randomized trials of antiviral-naïve patients that compared dual therapy with pegylated interferon alfa-2b plus ribavirin versus pegylated interferon alfa-2a plus ribavirin; triple therapy with pegylated interferon (alfa-2a or -2b), ribavirin, and either telaprevir or boceprevir versus dual therapy; or different doses or durations of dual or triple therapy. Dose and duration comparisons of dual therapy focused on genotype 2 or 3 infection. For the last question, EPC staff included cohort studies that reported adjusted risk estimates for the association between a sustained virologic response (SVR) after antiviral

treatment versus no SVR and clinical outcomes. Clinical outcomes were mortality, cirrhosis, hepatic decompensation, hepatocellular carcinoma, and need for transplantation. SVR, the primary intermediate outcome, was defined as the absence of detectable HCV ribonucleic acid (RNA) in the serum 6 months after the end of a course of therapy. Harms included withdrawals due to adverse events, serious adverse events, neutropenia, anemia, psychological adverse events, influenza-like symptoms, and rash.

EPC staff restricted inclusion to English-language articles and included studies published as conference abstracts only in sensitivity analyses. They excluded studies of pregnant women, patients who received a transplant, HIV-infected patients, patients undergoing hemodialysis, and previously treated patients. They excluded regimens with antiviral drugs not approved in the United States for HCV infection.

Mother-to-Infant Transmission

Data Sources and Searches

A research librarian searched Ovid MEDLINE (1947 to May 2012), EMBASE, the Cochrane Library Database, Scopus, PsycINFO, clinical trial registries (including clinicaltrials.gov), and grants databases. EPC staff supplemented electronic searches by reviewing reference lists of retrieved articles. Searches were peer reviewed by a second librarian.

Study Selection

At least 2 reviewers independently evaluated each study to determine inclusion eligibility. EPC staff selected for full-review randomized trials, cohort studies, and case-control studies that evaluated the association between mode of delivery (cesarean versus vaginal delivery), labor management strategies (use of internal fetal monitoring or management of premature rupture of membranes), or breastfeeding on risk for mother-to-infant transmission. EPC staff restricted inclusion to English-language articles and excluded studies published only as abstracts. Women co-infected with HIV are advised to avoid breastfeeding and deliver by elective cesarean if they are viremic in order to reduce risk for HIV transmission. Therefore, EPC staff excluded studies of HIV co-infected women, unless results for women not co-infected with HIV were reported separately or co-infected women made up less than 10% of the study sample.

Number of Source Documents

Screening

Sixteen studies were included in the synthesis:

- Yield of targeted screening strategies: 5 studies
- Harms of screening: 5 studies
- Harms of diagnostic liver biopsy: 6 studies

Treatment

Ninety studies were included in the synthesis:

- Key question 1a: 5 studies
- Key question 1b: 0 studies
- Key question 2a: 38 studies
- Key question 2b: 13 studies
- Key question 3a: 13 studies
- Key question 3b: 3 studies
- Key question 4: 28 studies

Mother-to-Infant Transmission

Eighteen studies were included in the synthesis.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): Systematic evidence reviews were prepared by the Oregon Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Screening

Data Abstraction and Quality Rating

One investigator abstracted details about the study design, patient population, setting, interventions, analysis, follow-up, and results. A second investigator reviewed data for accuracy. Two investigators independently applied predefined criteria to assess the quality of each study as good, fair, or poor. Discrepancies were resolved through a consensus process.

Data Synthesis

For studies reporting the diagnostic yield of different screening strategies, the number needed to screen to identify one case of hepatitis C infection (HCV) infection was computed by dividing the number of screening tests performed by the number of HCV cases identified. The proportion screened was the number of patients screened upon application of a particular screening strategy, divided by the total number of patients assessed.

EPC staff assessed the overall strength of each body of evidence as "high," "moderate," "low," or "insufficient" in accordance with the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews," based on the quality of studies, consistency between studies, precision of estimates, and directness of evidence.

Treatment

Data Extraction and Quality Assessment

One investigator abstracted details about the study design, population, setting, interventions, analysis, follow-up, and results. A second investigator reviewed data for accuracy. Two investigators independently applied predefined criteria to assess study quality as good, fair, or poor. Discrepancies were resolved through consensus.

Data Synthesis and Analysis

The overall strength of each body of evidence was assessed as "high," "moderate," "low," or "insufficient" in accordance with the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews" on the basis of the quality of studies, consistency between studies, precision of estimates, and directness of evidence.

EPC staff performed meta-analyses of trials that evaluated similar populations, interventions, comparisons, and outcomes to estimate pooled relative risks using the DerSimonian-Laird method in a random-effects model. Heterogeneity was assessed with the I^2 statistic. Statistical heterogeneity was explored through sensitivity and subgroup analyses based on study quality, differences in dosing or drugs, and outlier trials. Funnel plots were not produced because of small numbers of studies, but sensitivity analyses were performed that included studies published only as abstracts. Analyses were performed with Stata software, version 11.0 (StataCorp, College Station, Texas).

Mother-to-Infant Transmission

Data Extraction and Quality Rating

One investigator abstracted details about the study design, patient population, setting, interventions, analysis, follow-up, and results. A second investigator reviewed data for accuracy. Two investigators independently applied redefined criteria to assess the quality of each study as good, fair, or poor. Discrepancies were resolved through a consensus process.

Data Synthesis

EPC staff assessed the overall strength of each body of evidence as "high," "moderate," "low," or "insufficient" in accordance with the AHRQ "Methods Guide for Comparative Effectiveness Reviews," based on the quality of studies, consistency between studies, precision of estimates, and directness of evidence.

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

Table 1. U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

A, B, C, D, and I (*Insufficient*) represent the letter grades of recommendation or statement of insufficient evidence assigned by the U.S. Preventive Services Task Force after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the Task Force seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a general primary care population. For screening topics, this standard could be met by a large randomized, controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the Task Force considers indirect evidence. To guide its selection of indirect evidence, the Task Force constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

1. Do the studies have the appropriate research design to answer the key question(s)?
2. To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
3. To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
4. How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
5. How consistent are the results of the studies?
6. Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

The next step in the Task Force process is to use the evidence from the key questions to assess whether there would be net benefit if the service were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the Task Force's overall assessment of evidence was described as good, fair, or poor. The Task Force realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the Task Force has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term *certainty* will now be used to describe the Task Force's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the Task Force makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The Task Force must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The Task Force considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the Task Force assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The Task Force would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of the Recommendations" field). The Task Force would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion Documents" field) summarizes the current terminology used by the Task Force to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. *Ann Intern Med.* 2007;147:871-875.[5 references].

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the	Read the "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients

Grade	Grade Definitions	Suggestions for Practice
	balance of benefits and harms cannot be determined.	should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; or • Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; or • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review. Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary

organizations, and Federal agencies, as well as posted on the Task Force Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Response to Public Comments: A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 27 November to 24 December 2012. Some comments requested clarification about risk factors. Others addressed the costs of screening in the birth cohort and how hepatitis C virus treatment may be inaccessible to persons without health insurance coverage. Many comments noted that risk-based screening would be a burden to clinical providers, is viewed as less effective, and may be a low priority for clinicians who see asymptomatic patients. Many comments disagreed with the USPSTF's assessment of the benefits and harms of screening for hepatitis C virus in the birth cohort compared with high-risk persons.

In response to these comments, the USPSTF distinguished between established risk factors and less established risk factors in the Clinical Considerations section and added language about populations that are at risk. The USPSTF does not make recommendations on insurance coverage or assess or consider financial costs. The USPSTF also clarified how risk-based screening approaches may miss infected persons.

After the public comment period, the USPSTF considered new evidence that was published since its initial deliberation—specifically, studies by Kimer and colleagues, van der Meer and coworkers, Liu and associates, and Morgan and colleagues. After reviewing this new evidence, the USPSTF determined that the new studies support a moderate magnitude of net benefit for the birth cohort as well as for high-risk persons.

Comparison with Guidelines from Other Groups. Recommendations for screening from the following groups were discussed: The American Association for the Study of Liver Diseases, the Infectious Diseases Society of America, the American College of Gastroenterology, the U.S. Centers for Disease Control and Prevention, and the American Academy of Family Physicians.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Benefits of Detection and Early Intervention

- The U.S. Preventive Services Task Force (USPSTF) found no direct evidence on the benefit of screening for hepatitis C virus (HCV) infection in asymptomatic adults in reducing morbidity and mortality. However, the USPSTF found adequate evidence that antiviral regimens result in sustained virologic response and improved clinical outcomes.
- The USPSTF found inadequate evidence that counseling or immunization of patients with HCV infection against other infections improves health outcomes, reduces transmission of HCV, or changes high-risk behaviors. The USPSTF found inadequate evidence that knowledge of positive status for HCV infection reduces high-risk behaviors. The USPSTF also found inadequate evidence that labor management and breastfeeding strategies in HCV-positive women are effective at reducing risk for mother-to-child transmission.
- Given the accuracy of the screening test and the availability of effective interventions for HCV infection, the USPSTF concludes that screening is of moderate benefit for populations at high risk for infection. The USPSTF concludes that one-time screening in all adults in the United States born between 1945 and 1965 is also of moderate benefit.

Potential Harms

Harms of Detection and Early Intervention

- The U.S. Preventive Services Task Force (USPSTF) found limited evidence on the harms of screening for hepatitis C virus. Potential harms of screening include anxiety, patient labeling, and feelings of stigmatization.
- The USPSTF found adequate evidence on the harms associated with the diagnostic evaluation used to guide treatment decisions (liver

biopsy). These harms include bleeding, infection, and severe pain in approximately 1% of persons who had a liver biopsy and death in less than 0.2%. However, the use of liver biopsy to guide treatment decisions is declining, and noninvasive tests have sufficient accuracy to diagnose fibrosis and cirrhosis. Thus, the absolute risk to persons who currently receive a diagnosis of hepatitis C virus infection and subsequent treatment is probably declining.

- The USPSTF found adequate evidence that antiviral therapy regimens are associated with a high rate of harms, such as fatigue, headache, flu-like symptoms, hematologic events, and rash. However, antiviral therapy is given for a defined duration, serious adverse events are uncommon, and adverse events are self-limited and typically resolve after treatment is discontinued. The USPSTF found adequate evidence that these harms of treatment are small.

Contraindications

Contraindications

Antiviral therapy is contraindicated in pregnancy because of its potential teratogenic effects.

Qualifying Statements

Qualifying Statements

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.
- Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF will make all its products available through its [Web site](#) . The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size *Guide to Clinical Preventive Services*.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

U.S. Preventive Services Task Force. Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013 Sep 3;159(5):349-57. [20 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or its agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Guideline Committee

U.S. Preventive Services Task Force (USPSTF)

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**Members of the USPSTF at the time this recommendation was finalized. For a list of current Task Force members, go to <http://www.uspreventiveservicestaskforce.org/Page/Name/our-members> .*

Financial Disclosures/Conflicts of Interest

The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Potential Conflicts of Interest: Disclosure forms from USPSTF members can be viewed at

www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-1255 .

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Screening for hepatitis C virus infection in adults: recommendation statement. Ann Intern Med. 2004 Mar 16;140(6):462-4.

Guideline Availability

Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .

Availability of Companion Documents

The following are available:

Evidence Reviews:

- Chou R, Cottrell EB, Wasson N, Rahman B, Guise J-M. Screening for hepatitis C virus infection in adults: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Jan 15;158:101-108.
- Chou R, Cottrell EB, Wasson N, Rahman B, Guise J-M. Screening for hepatitis C virus infection in adults: Comparative effectiveness review No. 69. AHRQ Publication No. 12(13)-EHC090-EF. Rockville (MD): Agency for Healthcare Research and Quality; 2012 Nov. 370 p.
- Chou R, Hartung D, Rahman B, Wasson N, Cottrell EB, Fu R. Comparative effectiveness of antiviral treatment for hepatitis C virus infection in adults: a systematic review. Ann Intern Med. 2013 Jan 15;158:114-123.
- Chou R, Hartung D, Rahman B, Wasson N, Cottrell E, Fu R. Treatment for hepatitis C virus infection in adults: Comparative effectiveness review No. 76. AHRQ Publication No. 12(13)-EHC113-EF. Rockville (MD): Agency for Healthcare Research and Quality. 2012 Nov. 387 p.
- Cottrell EB, Chou R, Wasson N, Rahman B, Guise J-M. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Jan 15;158:109-113.

Electronic copies: Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .

Background Articles:

- Barton MB et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. Ann Intern Med 2007;147:123-127.
- Guirguis-Blake J et al. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Intern Med 2007;147:117-122.
- Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med 2007;147:871-875.

Electronic copies: Available from the [USPSTF Web site](#) .

The following are also available:

- Screening for hepatitis C virus infection in adults: clinical summary of U.S. Preventive Services Task Force recommendation. 2013 Jun. 1 p. Electronic copies: Available from the [USPSTF Web site](#) .
- The guide to clinical preventive services, 2012. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2012. 128 p. Electronic copies available from the [AHRQ Web site](#) . See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .
- Ngo-Metzger Q, Ward JW, Valdiserri RO. Expanded hepatitis C virus screening recommendations promote opportunities for care and cure. Ann Intern Med. 2013;159(5):364-365. Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .

The [Electronic Preventive Services Selector \(ePSS\)](#) is an application designed to provide primary care clinicians and health care teams timely decision support regarding appropriate screening, counseling, and preventive services for their patients. It is based on the current, evidence-based recommendations of the USPSTF and can be searched by specific patient characteristics, such as age, sex, and selected behavioral risk factors.

Patient Resources

The following are available:

- Screening for hepatitis C virus infection in adults. Understanding task force recommendations. Rockville (MD): U.S. Preventive Services Task Force. Consumer fact sheet. 2013 Jun. 4 p. Electronic copies: Available in Portable Document Format (PDF) from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .
- Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force Recommendation statement. Summary for patients. Ann Intern Med. 2013 Sep 3;159(5):I-32. Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .
- Women: stay healthy at any age. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 10-IP002-A. 2010 Aug. 2 p. Electronic copies: Available in Portable Document Format (PDF) in [English](#) and [Spanish](#) from the AHRQ Web site. See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .
- Men: stay healthy at any age. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 10-IP004-A. 2010 Aug. 2 p. Electronic copies: Available in PDF in [English](#) and [Spanish](#) from the AHRQ Web site. See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .

Print copies: Available in English and Spanish from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to <http://www.ahrq.gov/news/pubsix.htm> or call 1-800-358-9295 (U.S. only).

Myhealthfinder is a new tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the USPSTF and is available at www.healthfinder.gov .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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